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HIGHLY DISPERSE PREPARATION OF SILVER SALT OF SULFATHIAZOLE

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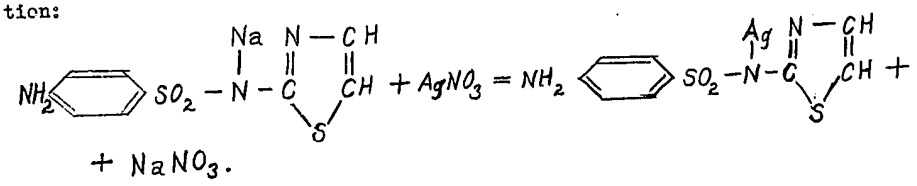
/Tables are appended./

The purpose of the present work has been to obtain a highly disperse preparation of the silver salt of sulfathiazole for local application.

According to published data, a colloidal dispersion of the silver salt of sulfathiazole is being used successfully in urology and otolaryngology. The preparation does not have an irritating effect on the mucous membranes of the nose, eyes, bladder, or other organs. The method for preparing a colloidal dispersion of this silver salt has received very little attention in scientific literature. Since methods for the preparation of a colloidal dispersion of the salt which have been described in literature are complicated, we endeavored to prepare it by a more practicable means. Two methods were possible: condensation and dispersion. However, the first method requires the presence of a suitable solvent for the silver salt, since the latter is insoluble in water and organic solvents. Therefore, we decided on the method of dispersion by means of exposure of the silver salt to the action of sound waves generated by a magnetostrictive oscillator.

The silver salt is obtained by the interaction of aqueous solutions of the sodium salt of sulfathiazole with silver nitrate. The reagents are taken in molecular proportions. This reaction proceeds according to the following equation:



$$+ NaNO_3.$$

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When prepared with mechanical agitation, the silver salt of sulfathiazole forms a coarse dispersion and, as a result, an unstable dispersed system. To increase the dispersion of the silver salt we varied the method of its preparation so that the silver nitrate solution was added to the solution of the sodium salt (1) under exposure to sound, (2) in the presence of a protective colloid, and (3) under exposure to sound accompanied by the addition of a protective colloid.

Microscopic observations showed that the dispersion of the silver salt increased only in case (3) above. To free the liquid of sodium nitrate produced in the process of the exchange reaction, it was filtered after having been exposed to sound, and the residue obtained in the form of a paste was washed with water.

To obtain a greater increase in dispersion, the washed paste was subjected to further sound treatment for 1, 2, 3, and 6 hours. Since it was discovered that only 2.4% more particles down to 1.5 μ were obtained with the 6-hour sound exposure than with the one-hour exposure, later experiments were conducted using the one-hour exposure.

In our experiments we used 0.5% pectin, since 1% so increased the viscosity that utilization was difficult. The addition of 0.5% pectin yielded satisfactory results in stabilizing and dispersing the preparation.

To characterize the dispersion of the preparation we employed sedimentation analysis, using a Figurov microbalance. Particle sizes were also determined microscopically, and for this operation the preparation was diluted with water in a 1:5 ratio.

To decide whether both stages -- silver salt and paste -- needed to be exposed to sound in the preparation of the dispersed silver salt, we tried (1) exposing both stages to sound, (2) agitating the first stage with a mixer and exposing the second to sound, and (3) agitating both stages with a mixer.

In the first case, 42.2% of the particles were smaller than 0.7 μ, in the second 17.9%, and in the third 10.7%. From these data it follows that when both stages are exposed to sound we obtain a dispersion with a greater content of fine particles than when only the second stage is exposed, while more fine particles are obtained when only the second stage is exposed to sound than when both stages are agitated with a mixer (Table 1).

The data in Table 1 were also confirmed microscopically. When both stages were exposed to sound, the whole field of vision under the microscope was filled with particles up to 1.5 μ in size, particles larger than 12 μ being rarely encountered. When only the second stage was exposed to sound, the field of vision was partially filled with particles of 35 μ, while when both stages were agitated with a mixer part of the field was filled with particles of 75 μ.

However, dispersions obtained by the exposure of both stages contained 12-18% of particles of a size larger than 7.5 μ, which could not help but be reflected in their stability. Experiments have shown that the dispersion can be freed of 50% of these large particles by allowing it to stand for 10 days (Table 2).

The best results were obtained by centrifuging. After centrifuging a dispersion of the silver salt of sulfathiazole for 7 hours at 3,000 rpm, an almost transparent liquid was obtained in which there were no particles larger than 0.5 μ.

In the search for methods to preserve the preparation for a long time, it was dried under different conditions: (1) at room temperature; (2) under slight heating in vacuum; and (3) by freezing out, in the manner by which unstable substances are dried. Only the preparation which was dried by the last method preserved its original dispersion, as is confirmed by data from sedimentation analyses before and after drying.

Drying of the preparation must be carried out under conditions of freezing, since at higher temperatures the pectin apparently loses its protective properties, and this leads to the aggregation of particles. In a number of experiments the growth of the relative content of fine fractions after drying could be noticed (Table 3). Evidently the disaggregation of particles is accompanied by a partial dehydration of the pectin.

On the basis of our data, the following method for obtaining the preparation was developed. To an aqueous solution of the silver salt of sulfathiazole, in the presence of a protective colloid (pectin), a solution of silver nitrate is added gradually in a molecular ratio, accompanied by exposure to sound from a magnetostrictive oscillator. When the addition of silver nitrate has been completed, the liquid is filtered in a Buechner funnel under vacuum and the residue, obtained in the form of a paste, is washed with water to remove the sodium nitrate. This paste of the silver salt of sulfathiazole, diluted with water to a 15% content of the salt, is then exposed to sound in the presence of the same protective colloid. A preservative is then introduced into the preparation. The obtained highly disperse preparation of the silver salt of sulfathiazole is a viscous liquid, white or rose in color, depending on the color of the pectin.

The following conclusions are drawn:

1. A highly disperse preparation of the silver salt of sulfathiazole is obtained by exposure to sound waves from a magnetostrictive oscillator in the presence of a protective colloid (pectin).

2. A more highly disperse preparation is obtained by exposure to sound waves than by agitation with a mixer.

3. Upon being dried, subsequently to freezing out, the preparation preserves its original degree of dispersion.

[Appended tables follow:]

Table 1. Effect on the Degree of Dispersion of the Method of Preparing Silver Salt of Sulfathiazole

Method of Dispersion		Content of Particles of Different Sizes (in %)				
		Sizes of Particles (in μ)				
Silver Salt	Paste	To 0.7	0.7-1.5	1.5-4.5	4.5-7.5	7.5 and Greater
Exposure to sound	Exposure to sound	4.24	17.1	21	7.5	12
Agitation with mixer	Exposure to sound	17.9	14.5	44.5	11.8	11.3
Agitation with mixer	Agitation with mixer	10.7	13.8	47.0	10.5	18

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Table 2. Data From Sedimentation Analysis Before and After Standing

No of Expt	Duration of Standing (in days)	Content of Particles of Different Sizes (in %)			
		Sizes of Particles (in μ)			
		To 1.5	1.5-4.5	4.5-7.5	7.5 and Greater
4	--	34.5	39.9	6.7	18
5	10	52	31	5	12

Table 3. Data From Sedimentation Analysis Before and After Drying

No of Expt	Moment of Time	Content of Particles of Different Sizes (in %)			
		Sizes of Particles (in μ)			
		To 1.5	1.5-4.5	4.5-7.5	7.5 and Greater
6	Before Drying	20	24.5	16.6	38.9
	After Drying	61.4	25.9	5.0	7.7
7	Before Drying	35.5	38.4	9.4	16.7
	After Drying	58.7	17.8	8.5	15

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